

**Amendments to the Claims**

Please amend claims 1, 80, and 81, as set forth below in the Listing of Claims.

Please cancel claim 14.

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1. (Currently amended) A method of identifying an agent that inhibits reverse transcriptase comprising:

- a) contacting a cell comprising a divalent cation transporting protein with a test agent;
- b) detecting a change in the concentration of intracellular manganese ions in the cell after contact with the test agent as compared to the concentration of manganese ion levels in the absence of the test agent[.]; and
- c) detecting reverse transcriptase activity in the cell using a polyribonucleotide or polydeoxyribonucleotide template for reverse transcriptase activity, wherein an increase in the concentration of intracellular manganese ions in the cell after contact with the test agent, and a decrease in activity of reverse transcriptase is indicative of an agent that inhibits reverse transcriptase.

2. (Previously presented) The method of claim 1, wherein the cell comprises an isolated cell membrane.

3. (Previously presented) The method of claim 2, wherein the cell membrane comprises a eukaryotic cell membrane.

4. (Original) The method of claim 3, wherein the eukaryotic cell membrane comprises a yeast cell membrane or a mammalian cell membrane.

5. (Original) The method of claim 3, wherein the eukaryotic cell membrane comprises a human cell membrane.

6. (Previously Presented) The method of claim 1, wherein contacting the cell comprises contacting a cell comprising a cell membrane.

7. (Original) The method of claim 6, wherein the cell comprises a yeast cell.

8. (Original) The method of claim 6, wherein the cell comprises a human cell.

9. (Original) The method of 6, wherein the cell comprises a T lymphocyte.

10. (Previously presented) The method of claim 1, wherein the cell comprises a divalent cation transport protein comprising a P-type ATPase.

11. (Original) The method of claim 10, wherein the ATPase is a Pmr1p protein or a homolog thereof.

12. (Previously presented) The method of claim 1, wherein the test agent does not alter transport of a divalent cation other than manganese ions by a divalent cation transporting protein.

13. (Original) The method of claim 1, wherein the agent reduces or inhibits manganese ion transport out of a cell.

Claims 14-20. (Canceled)

21. (Withdrawn) An agent identified according to the method of claim 1, wherein the agent modulates reverse transcriptase activity in a cell.

22. (Withdrawn) A method of identifying an agent that modulates reverse transcriptase activity in a cell, comprising:
- contacting a cell expressing a reverse transcriptase with a test agent; and
  - detecting altered reverse transcriptase activity due to contact with the test agent as compared to reverse transcriptase activity in the absence of the test agent, wherein the test agent alters manganese ion concentration in the cell, thereby identifying an agent that modulates reverse transcriptase activity in a cell.
23. (Withdrawn) The method of claim 22, wherein detecting reverse transcriptase activity comprises measuring cDNA produced by the reverse transcriptase using a polynucleotide template in the cell.
24. (Withdrawn) The method of claim 23, wherein the polynucleotide template comprises a retrotransposable element.
25. (Withdrawn) The method of claim 24, wherein the retrotransposable element comprises a transposon.
26. (Withdrawn) The method of claim 25, wherein the transposon comprises a Ty transposon.
27. (Withdrawn) The method of claim 26, wherein the Ty transposon comprises a Ty-1 transposon.
28. (Withdrawn) The method of claim 24, wherein the retrotransposable element comprises a retrovirus.
29. (Withdrawn) The method of claim 22, wherein the reverse transcriptase comprises a retrovirus reverse transcriptase.

30. (Withdrawn) The method of claim 29, wherein the retrovirus reverse transcriptase comprises a human immunodeficiency virus reverse transcriptase or an avian myeloblastosis virus reverse transcriptase.

31. (Withdrawn) The method of claim 22, wherein the cell comprises a yeast cell, an avian cell, or a mammalian cell.

32. (Withdrawn) The method of claim 22, wherein the cell comprises a *Saccharomyces cerevisiae* cell.

33. (Withdrawn) The method of claim 22, wherein the cell comprises a human cell.

34. (Withdrawn) The method of claim 22, which is performed in a high throughput format, wherein the cell comprises one of a plurality of cells.

35. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is the same or different, or a combination thereof.

36. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is arranged in an array.

37. (Withdrawn) The method of claim 36, wherein the array is an addressable array.

38. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is on a microchip, on a glass slide, on a bead, or in a well.

39. (Withdrawn) The method of claim 34, wherein each of the cells of the plurality is contacted with a test agent, which is the same or different or a combination thereof.

40. (Withdrawn) The method of claim 34, wherein the cell is a yeast cell, said plurality of cells comprising a plurality of yeast cells.

41. (Withdrawn) The method of claim 40, wherein the yeast cell expresses a human divalent cation transporting protein.

42. (Withdrawn) The method of claim 41, wherein the human divalent cation transporting protein comprises a human Pmrp1 transporting protein.

43. (Withdrawn) The method of claim 22, wherein the cell comprises a sample obtained from a subject.

44. (Withdrawn) An agent identified according to the method of claim 22, wherein the agent modulates reverse transcriptase activity in a cell.

45. (Withdrawn) A method of modulating reverse transcriptase activity in a cell, comprising contacting the cell with an agent that alters manganese ion transport across a cell membrane of the cell, thereby modulating reverse transcriptase activity in the cell.

46. (Withdrawn) The method of claim 45, wherein the agent reduces or inhibits manganese ion transport out of the cell.

47. (Withdrawn) The method of claim 45, wherein the agent that alters manganese ion transport does not alter transport of a divalent cation other than manganese ion.

48. (Withdrawn) The method of claim 45, wherein the agent alters the activity of a divalent cation transporting protein in a cell membrane of the cell.

49. (Withdrawn) The method of claim 48, wherein the divalent cation transporting protein comprises a P-type ATPase.

50. (Withdrawn) The method of claim 49, wherein the P-type ATPase comprises a Pmr1p protein or a homolog thereof.

51. (Withdrawn) A method of modulating reverse transcriptase activity, comprising contacting a reverse transcriptase with a predetermined concentration of manganese ions, thereby modulating reverse transcriptase activity.

52. (Withdrawn) The method of claim 51, further comprising contacting the reverse transcriptase with a predetermined concentration of magnesium ions.

53. (Withdrawn) The method of claim 51, wherein modulating the reverse transcriptase activity comprises increasing relative reverse transcriptase activity for a polyribonucleotide template as compared to a polydeoxyribonucleotide template.

54. (Withdrawn) The method of claim 51, wherein the reverse transcriptase is a human immunodeficiency virus reverse transcriptase.

55. (Withdrawn) A method of ameliorating a retrovirus infection in a subject, comprising administering an agent that alters manganese ion transport in a retrovirus infected cell of the subject, thereby ameliorating the retrovirus infection.

56. (Withdrawn) The method of claim 55, wherein the agent reduces or inhibits a divalent cation transporting protein activity in the retrovirus infected cell.

57. (Withdrawn) The method of 56, wherein the agent does not alter transport of a divalent cation other than a manganese ion by the divalent cation transporting protein.

58. (Withdrawn) The method of claim 56, wherein the divalent cation transporting protein comprises a Pmr1p protein or a homologue thereof.

59. (Withdrawn) The method of claim 55, wherein the subject is a human subject.

60. (Withdrawn) The method of claim 55, wherein the retrovirus infected cell comprises a human T lymphocyte.

61. (Withdrawn) A high throughput assay for identifying an agent that alters manganese ion transport by a divalent cation transporting protein in a cell, comprising an array comprising a plurality of cells that express a heterologous divalent cation transporting protein, wherein the heterologous divalent cation transporting protein transports at least manganese ion.

62. (Withdrawn) The high throughput assay of claim 61, wherein the plurality of cells comprises a plurality of yeast cells.

63. (Withdrawn) The high throughput assay of claim 62, wherein the heterologous divalent cation transporting protein comprises a human divalent cation transporting protein.

64. (Withdrawn) The high throughput assay of claim 63, wherein the human divalent cation transporting protein comprises a human Pmrp1 transporting protein.

65. (Withdrawn) The high throughput assay of claim 61, wherein the array comprises an array of wells, wherein cells of the plurality are contained in the wells.

66. (Withdrawn) The high throughput assay of claim 61, wherein cells of the plurality of cells further express a reporter gene.

67. (Withdrawn) The high throughput assay of claim 66, wherein expression of the reporter gene in a cell of the plurality is regulated by manganese ion concentration in the cell.

68. (Withdrawn) The high throughput assay of claim 66, wherein expression of the reporter gene in a cell of the plurality is regulated by reverse transcriptase activity in the cell.

69. (Withdrawn) A method of identifying an agent that modulates reverse transcriptase activity in a cell, comprising:

contacting cells of an array of cells with at least one test agent, wherein the cells comprise a divalent cation transporting protein, which transports manganese ions; and  
detecting altered manganese ion transport in cells of the array due to contact with the test agent as compared to manganese ion transport in the absence of the test agent, thereby identifying an agent that modulates reverse transcriptase activity in a cell.

70. (Withdrawn) The method of claim 69, wherein cells of the array are eukaryotic cells.

71. (Withdrawn) The method of claim 70, wherein the eukaryotic cells are yeast cells or mammalian cells.

72. (Withdrawn) The method of claim 69, wherein the divalent cation transporting protein expressed by the cells of the array is a heterologous divalent cation transporting protein transports.

73. (Withdrawn) The method of claim 72, wherein the cells of the array comprise yeast cells.

74. (Withdrawn) The method of claim 72, wherein the heterologous divalent cation transporting protein comprises a human divalent cation transporting protein.



75. (Withdrawn) The method of claim 74, wherein the human divalent cation transporting protein comprises a human Pmrp1 transporting protein.

76. (Canceled)

77. (Previously presented) The method of claim 1, wherein the agent increases manganese ion transport into a cell.

78. (Previously presented) The method of claim 1, wherein the cell comprises a divalent cation transport protein comprising an ATPase.

79. (Withdrawn) A method of identifying an agent that inhibits reverse transcriptase comprising:

- a) contacting a cell comprising a divalent cation transporting protein with a test agent;
- b) detecting a change in the concentration of intracellular manganese ions in the cell after contact with the test agent as compared to the concentration of manganese ion levels in the absence of the test agent; and
- c) detecting inhibition of retrotransposable element replication, thereby identifying the agent as an inhibitor of reverse transcriptase.

80. (Withdrawn – Currently Amended) The method of claim [[79]] 1, wherein the polyribonucleotide or polydeoxyribonucleotide template comprises a nucleotide sequence of a [[the]] retrotransposable element, and wherein further the retrotransposable element is a human immunodeficiency virus [Human Immunodeficiency Virus] (HIV).

81. (Withdrawn – Currently Amended) The method of claim [[79]] 1, wherein the polyribonucleotide or polydeoxyribonucleotide template comprises a nucleotide sequence of a [[the]] retrotransposable element, and wherein further the retrotransposable element is a Ty[[1]] retrotransposon.